Genomic analysis of *Acinetobacter baumannii* prophages reveals remarkable diversity and suggests profound impact on bacterial virulence and fitness

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Acinetobacter baumannii has been recently indicated by the World Health Organization (WHO) as the number one priority pathogen for research and development of new antibiotics. This is a direct consequence of the fast evolution of pathogenicity, and in particular of multidrug resistance, of this nosocomial pathogen.

While the development of new antibiotics is critical, understanding the mechanisms behind the crescent pathogenicity of this bacterium is equally relevant. Often, resistance and other virulence elements of pathogenic bacteria are contained on highly mobile pieces of DNA that can easily spread to other bacteria by a process of horizontal gene transfer (HGT). Among mediators of HGT we find bacteriophages (phages), viruses of bacteria thought to be the most abundant entities on Earth. When infecting a bacterial host, phages may follow a lytic path in which they replicate inside the bacteria and cause cell lysis for progeny release, or they may follow a lysogenic life cycle where they integrate the host genome and replicate in synchrony. Phages opting for the lysogenic life cycle are known as temperate phages, or prophages when integrated in the bacterial genome. Under certain stimuli prophages can excise from the host genome, entering the lytic cycle and resulting in cell death and release of phage progeny. During excision, a process of specialized transduction may occur, where parts of the bacterial genome adjacent to the prophages may be erroneously excised with the prophage genome and introduced with the virion into a new host. Often these pieces of DNA offer advantageous features to the bacterial host, as exemplified by the well-known prophage-encoded Shiga toxin of *Escherichia coli* O157:H7.

So here we question the contribution of prophages to the evolution of *A. baumannii* pathogenicity. We found prophages to be widely disseminated in 959 *A. baumannii* genomes, with a few also present in bacterial plasmids. Whole genome and proteome comparisons demonstrated a notable diversity of prophage sequences, with only a few small clusters of closer evolutionary relationships. Also remarkably, *A. baumannii* prophages encode for a multitude of putative virulence factors that may be implicated in the bacterium's capacity to colonize host niches, evade the host immune system, subsist in unfavorable environments, and tolerate antibiotics, including last resource agents as colistin.

Overall, our results point towards a significant contribution of prophages for the dissemination and evolution of pathogenicity in *A. baumannii*, and highlight the clinical relevance of these mediators of HGT.